REMARKS

Status of the Application and the Present Response

Prior to entry of the present Response, claims 1-9, 11-13, 22-28, 33-41, 43-59 and 61-74 were pending in the application, with claims 33-41, 43-59 and 61-74 being withdrawn from the application as directed to non-elected inventions. With entry of the instant response, claims 38, 38, 39, 58 and 59 have been canceled. In addition, claims 1, 11-13, 46, 56, 57, 63, 64, and 73 have been currently amended. The claims have also been amended to make it clearer that the reporter gene and the target polypeptide are expressed from two separate nucleic acid constructs. Support for these amendments is replete in the specification, e.g., in paragraphs 57 and 73. In addition, claim 1 has been amended to specify that host cell is an E. coli cell. Unless otherwise noted, the amendments made herein are intended to improve clarity or expedite prosecution, and should not be construed as acquiescence of any ground of rejections.

The instant Office Action maintained the rejection of the pending claims as allegedly failing to comply with the written description requirement. In addition, new grounds of rejections were also set forth in the Office Action. The following remarks address these and other issues raised in the instant Office Action.

Rejection under 35 U.S.C. § 112 - Written Description

Claims 1-9, 11-13, 22-27 and 33 remain rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. In essence, the rejection was maintained on the alleged ground that the disclosure does not adequately describe identifying characteristics that would be representative of the genus of protein solubility responsive promoters. In addition, the instant Office Action further alleged that there is inadequate written description with regard to the recitation of a host cell. It was stated in the Office Action that "the skilled artisan would not view the disclosure as providing adequate descriptive support for the claimed invention beyond the scope of an *E. coli* host cell." Applicants respectfully traverse this rejection for the reasons stated below.

Applicants respectfully disagree with the Examiner's assertion that the subject disclosure does not provide adequate description of host cells beyond the scope of an E. coli host cell. Nevertheless, in an additional effort to expedite

prosecution of the subject patent application which has been pending for a few years, Applicants have herein further amended the claims. The host cells recited in the claims are now limited to E. coli cells. Therefore, this newly asserted ground of the rejection has been obviated.

Applicants maintain that the subject disclosure meet the written description requirement with respect to the recitation of protein solubility responsive promoters in the rejected claims. Applicants urge the Examiner to note the material differences between the presently rejected claims and hypothetical claims that are directed to protein solubility responsive promoters per se. Applicants acknowledge that, as stated in the MPEP, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species" (MPEP §2163.05-I; emphasis added). For a hypothetical claim that is directed to a genus of protein solubility responsive promoter per se, the structural information of the promoter would be an essential element. For such a claim, it might be reasonable to require that the structural information of the disclosed species be representative of the entire genus. However, it must be emphasized that the presently rejected claims are not directed to a genus of protein solubility responsive promoters. Rather, the presently claimed invention (e.g., claim 1) is directed to host cells which harbor a protein promoter solubility responsive promoter for examining solubility of a target protein, and to methods employing such host cells. Unlike the hypothetical claim, the employed promoter is not an essential element of the claimed invention on which patentability is predicated. So long as the promoter is responsive to expression of an insoluble protein in the host cell, the exact nature or identity (e.g., structural information) of the employed promoter is inconsequential to the practice of the claimed invention.

The distinction between these two types of claims noted above can be further described in another way. To satisfy the written description requirement for claims directed to a genus of protein solubility responsive promoters per se, the "identifying characteristics" of disclosed species might need to include structural information that is representative of the entire genus. However, the same should not be applied to claims directed to methods or compositions that merely employ a protein solubility responsive promoter to assess solubility of a target polypeptide. Here, it should not be the structural or sequence information of the disclosed species

that must be representative of the entire genus in order to satisfy the written description requirement. Rather, it is the ability of the disclosed promoters to be responsive to expression of insoluble proteins that need to be representative of the entire genus. Such ability of the disclosed E. coli protein solubility responsive promoters in the subject specification is surely representative of the entire genus of E. coli protein solubility responsive promoters.

The case in point is quite analogous to an example described in the MPEP, at § 2163-II-A-3-(a)-ii). There, citing *In re Rasmussen* (650 F.2d 1212, 1214, 211 USPQ 323, 326-27 (CCPA 1981) as an example), the MPEP notes that "there may be situations where one species adequately supports a genus." In *Rasmussen*, the court held that "disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to 'adheringly applying' because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered." Applying the same rational to the instant case, Applicants have provided a number of protein solubility responsive promoters which are capable of responding to expression of insoluble proteins. These disclosed species satisfy the written description requirement for the claimed methods because the exact sequence of the protein solubility responsive promoter is not important so long as they can respond to expression of insoluble proteins.

For all the reasons stated above and in Applicants' previously filed responses, Applicants submit that the subject specification has undoubtedly provided adequate description of the presently claimed invention. Accordingly, Applicants respectfully request that the instant rejection be withdrawn.

Rejection under 35 U.S.C. § 112 - Indefiniteness

Claim 33 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly as allegedly being indefinite. It was stated in the Office Action that the recitation of "a mutated form a polypeptide" renders the claim indefinite because there is no definition of what constitutes a mutated form of a polypeptide. Applicants respectfully disagree. To a skilled person in the art of biochemistry and molecular biology, the meaning of a mutated polypeptide should be apparent in any given context. For example, one would understand that a mutated polypeptide is relative to the wildtype form of the molecule that naturally exists in a wildtype host that harbors

the molecule. The mere existence of many possible mutated forms of a polypeptide does not render the recited term indefinite. Applicants should not be required to provide definition of a term that is well understood in the relevant arts. It is neither reasonable nor possible for applicants to set forth all possible mutant forms of a polypeptide. Accordingly, Applicants respectfully request that the instant rejection be withdrawn.

Double Patenting

Claim 1 stands provisionally rejected and claims 2-9, 11-13, 22-28 and 33 are newly rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1, 2 and 4-14 of co-pending application 10/127,078.

Applicants reiterate their willingness to address these provisional rejections once claims in the co-pending applications have been issued.

Rejection under 35 U.S.C. § 102

Claims 1, 5, 8, 11, 13, 22-28 and 33 are rejected as allegedly anticipated by Farr et al. (US Patent No. 5,589,337). It was asserted that in the Office Action that "the host cells of Farr et al. does comprise a target polypeptide heterologous to the host cell," and that "Far et al. teaches that the host cells are transformed with reporter constructs comprising an ampicillin resistance gene and a lacZ gene" that are not endogenous to the host cells. It was further stated in the Office Action that the ampicillin resistance gene and lacZ gene in Farr et al. meet the limitations of the target polypeptide-expressing nucleic acid of the presently claimed invention.

Applicants respectfully disagree the reasoning underlying the instant rejection. Even assuming for the sake of argument that the ampR and lacZ genes in Far et al. are not endogenous to the host cells, they are not target polypeptide-expressing nucleic acid as recited in the presently claimed invention. As described in Farr et al., the lacZ gene and ampicillin resistance gene are part of the cloning vector pRS415 into which the stress promoter is cloned (Col. 20, lines 1-18). Thus, these genes are located in the same construct that harbors the stress promoter and the reporter gene. On the other hand, the target polypeptide-expressing nucleic acid in

the presently claimed host cells is located in a separate nucleic acid construct that is independent of the construct that harbors the solubility promoter and the reporter gene.

To further improve clarity of the claim language, Applicants have herein amended the claims to more clearly specify that the solubility promoter/reporter gene and the polynucleotide expressing the target polypeptide are present on two separate nucleic acid constructs. The host cells in Farr et al. do not harbor both a first construct expressing a reporter gene from a solubility promoter and a second construct expressing a target polypeptide heterologous to the host cell. Therefore, the presently claimed invention is novel over Farr et al. since Farr et al. does not each element of the presently claimed invention. Accordingly, the instant claim rejection should be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 1-8, 11, 13, 22-28 and 33 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Farr et al. in view of Allen et al. (J. Bacteriol. 174: 6938-47, 1992). The Office Action alleged that Farr et al. taught the claimed invention except for the specific solubility responsive genes recited in claims 2, 3, 6 and 7, that Allen et al. taught the promoter region of the E. coli ibpA gene, and that it would be obvious for one to combine teachings from these two references. The Office Action then concluded that the combined disclosures from the cited art render the claims obvious. Applicants respectfully traverse this rejection.

There are three basic elements that must be met to establish prima facie obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

In the instant case, a prima facie case of obviousness of the presently claimed invention has not and could not be established. First, the cited references, standing alone or in combination, do not teach or suggest each and every element of

the claimed invention. As noted above, Farr et al. do not teach or suggest host cells which harbor both a first construct expressing a reporter gene from a solubility promoter and a second construct expressing a target polypeptide. While Allen et al. might have described heat shock genes including IbpA, this reference does not remedy the deficiency of Farr et al. Thus, even assuming one might be motivated to combine the teachings of the cited references, he would still not be led to the presently claimed invention.

In addition, there would not have been motivation or suggestion to combine teachings of the cited references and that of any other art that might render the subject invention obvious. This is because Farr et al. expressly taught away from the presently claimed invention. For example, after indicating that preferably the host cell strain should be homologous with the stress promoter, Farr et al. further stated that "the strain should also be wild type for all other genes, *especially stress genes*" (Col. 12, lines 33-41; emphasis added). Thus, Farr et al. explicitly suggest to the readers that their host cell and solubility reporter construct system should not be used with exogenous stress genes.

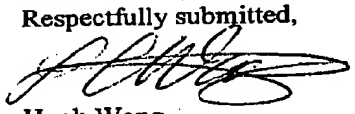
For at least the reasons stated above, Applicants submit that claims 1-8, 11, 13, 22-28 and 33 as presently amended are non-obvious and patentable over the cited art. Accordingly, Applicants respectfully request that the instant rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned attorney at 858-812-1539.

Respectfully submitted,



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